REMARKS

Rejection Under 35 USC 103(a)

Claims 82-87 and 91-100 have been rejected under 35 USC 103(a) as being unpatentable over Mouritsen et al. (WO 95/05849) in view of van der Zee et al. (Vaccine Vol. 13, No. 8, pages 753-758, 1995). More specifically, the Patent Office states:

> ...it would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify ubiquitin fusion proteins disclosed by Mouritsen et al. to use GnRH as the self epitope as disclosed by van der Zee et al. since GnRH is considered the pivotal regulatory peptide in mammalian reproduction and there is a demand for an effective, low cost means of controlling fertility in domestic animals...the ability of ubiquitin to generate an immune response to a self epitope is an inherent characteristic of the fusion protein...

Claims 82 and 97-100 have been amended to introduce the limitation that the ubiquitin-fusion protein of said claims consists essentially of endogenous self-epitopes. The amendment thereby obviates the rejection of said claims. Mouritsen et al. teach the incorporation of one or more T-cell epitopes into the highly conserved self-protein ubiquitin. Mouritsen et al. disclose one ubiquitin fusion protein containing the T-cell epitope ovalbumin (OVA 325-336) and another containing the T-cell epitope HEL 50-61. van der Zee et al. teach a fusion protein containing GnRH fused to the T-cell epitope *P. fimbriae*. In both references cited, foreign epitopes are essential elements in the fusion proteins for generating immune responses. A ubiquitin fusion protein consisting essentially of endogenous self-epitopes is neither implicitly nor explicitly suggested in either 1) the knowledge of one of skill in the art or 2) the combination of cited references. Motivations such as increased stabilization, increased efficiency of translation, and increased preservation of biological activity due to proper folding associated with ubiquitin fusion proteins are insufficient to arrive at Applicant's invention of the current claims, as amended,

since both references, as well as the state of the art at the time of Applicant's filing, suggest that the claimed combination would not generate an immune response.

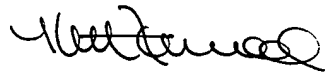
Prior to the present invention, ubiquitin fusions were not recognized in the art as being immunogenic for self-epitopes fused to ubiquitin protein. One of skill in the art would not have expected a ubiquitin fusion to generate an immune response to a self-epitope in a protein fusion since ubiquitin itself is highly conserved. Although Mouritsen et al. teach the incorporation of one or more T-cell epitopes into the highly conserved self-protein ubiquitin and disclose that "the antibody response induced (to the fusion protein) is not necessarily restricted to the inserted T-cell epitope (page 6, lines 33-35)," Applicant submits that the recognition of the ability of a fusion protein to generate antibodies to ubiquitin is not a disclosure or suggestion that a ubiquitin fusion protein consisting essentially of endogenous self epitopes is immunogenic. Mouritsen et al. does not disclose nor suggest the immunogenic property of ubiquitin fused to a self-epitope.

Applicant submits that amended Claims 82-87 and 91-100 of the instant application claim profoundly different methods for stimulating an immune response, methods which include providing a ubiquitin fusion protein consisting essentially of endogenous self epitopes, wherein the ubiquitin fusion is immunogenic for the non-ubiquitin self-epitopes therein.

Summary

In light of the above amendment, consideration of the subject patent application is respectfully requested. Any deficiency or overpayment should be charged or credited to Deposit Account No. 500282.

Respectfully submitted,



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